MANAGEMENT OF ONCOLOGIC EMERGENCIES

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November 2019

- Oncologic emergencies can occur as an initial manifestation of cancer, as a side effect
- of therapy, or at the time of progression or recurrence of the disease.
- Excellent cancer management requires mastery of the following:
- • Metabolic emergencies including hyperleukocytosis, tumor lysis syndrome (TLS), and associated electrolyte
- derangements.
- • Cardiothoracic emergencies including superior vena cava syndrome and mediastinal masses.
- • Acute abdominal processes.
- • Renal dysfunction and hypertension.
- • Neurologic emergencies.
- • Endocrine emergencies.
- • Treatment-related emergencies.

METABOLIC EMERGENCIES

- Hyperleukocytosis
- Hyperleukocytosis is defined as a total white cell count greater than 100,000/mm3. Hyperleukocytosis is seen
- at presentation in 9-13% of children with acute lymphocytic leukemia (ALL) and 5-22% of children with acute myeloid leukemia (AML).
- It occurs in an even higher percentage of patients with chronic myeloid leukemia (CML).

- The presence of a high number of blasts in the microcirculation leads to sludging, which interferes with oxygenation of local tissue, ultimately leading to tissue ischemia. This in turn leads to an adhesive reaction between abnormal vascular endothelium and the circulating blasts worsening leukostasis, thrombosis, and leading to secondary hemorrhage.
- The higher metabolic rate of the blasts and the local production of cytokines also contribute to tissue hypoxia. Thrombi in the circulation lead to vascular damage and parenchymal ischemia manifested as pulmonary or cerebrovascular hemorrhage and edema.
- Myeloblasts are larger, less deformable, and more adherent to vasculature than lymphoblasts. Due to these intrinsic properties, leukostasis and thrombosis are far more prevalent in AML than in ALL. At presentation,
- patients with AML are more likely to have intracranial hemorrhage or thrombosis or pulmonary hemorrhage and leukostasis, whereas ALL is more likely to lead to metabolic disturbance from tumor lysis syndrome.

- As leukostasis is associated with early morbidity and mortality, any patient presenting with a white blood cell
- count greater than 50,000/mm 3 should be evaluated closely for clinical signs and symptoms of leukostasis.

◦ Clinical Features

◦ • Central nervous system (CNS): blurred vision, confusion, somnolence, delirium, stupor, coma and papilledema.

◦ • Computed tomography (CT) may reveal hemorrhage or leukemic infiltrate.

◦ • Pulmonary: tachypnea, dyspnea, hypoxia.

◦ • Chest radiograph may reveal varying degree of diffuse interstitial or alveolar infiltrates.

◦ • Genitourinary: oliguria, anuria, rarely priapism.

◦ • Vascular symptoms which include disseminated intravascular coagulation (DIC), retinal hemorrhage,

◦ myocardial infarction, and renal vein thrombosis.

- Risk Factors
- • WBC counts .200,000/mm3 in AML, and .300,000/mm3 in ALL and CML.
- • Age less than 1 year.
- • M4, M5 AML (higher lysozyme activity).
- • Cytogenetic abnormalities including MLL 11q23, t(4:11), inv16, Philadelphia positive, and Philadelphia-like
- ALL and FLT3-ITD.

Tumor Lysis Syndrome

TLS arises due to the rapid release of intracellular metabolites (such as phosphorous, potassium, and uric acid) from dying tumor cells in quantities that exceed the excretory capacity of the kidneys.

In patients with a high tumor burden or rapid cell proliferation, such as Burkitt or Burkitt-like lymphoma, B-cell ALL, and T-cell leukemia or lymphoma, significant cell death and release of intracellular ions, even prior to chemotherapy initiation, may result in the following metabolic complications:

- Hyperuricemia.
- Hyperkalemia.
- Hyperphosphatemia.
- Hypocalcemia.
- Renal insufficiency/failure.

If not successfully treated, TLS can result in cardiac arrhythmias, renal failure, seizures, coma, DIC, and death.

- Diagnostic Criteria for Laboratory TLS and Clinical TLS
- Laboratory TLS (LTLS): The presence of two or more abnormal serum values at presentation (i.e., uric acid
- ≥8 mg/dl, potassium ≥6 mg/dl, phosphate ≥2.1 mmol/l, calcium ≤1.75 mmol/l, creatinine >normal).
- Clinical TLS (CTLS): Presence of LTLS and one or more of the following clinical complications: renal insufficiency, cardiac arrhythmias, seizures or sudden death.

TABLE 32.1 Patient Stratification by Risk for TLS for Various Types of Cancer

Type of cancer	Risk		
	High	Intermediate	Low
NHL	Burkitt, lymphoblastic	DLBCL	Indolent NHL
ALL	WBC $\geq 100{,}000/mm^3$	WBC $50{,}000–100{,}000/mm^3$	WBC $\leq 50{,}000/mm^3$
AML	WBC $\geq 50{,}000/mm^3$	WBC $10{,}000–50{,}000/mm^3$	WBC $\leq 10{,}000/mm^3$
Other hematologic malignancies (including CML) and solid tumors		Rapid proliferation with expected rapid response to therapy	Remainder of patients

NHL, non-Hodgkin's lymphoma; DLBCL, diffuse large B-cell lymphoma; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia.

Source: Reproduced with permission from Coiffier et al., 2008.

- Prevention and Management of TLS
- Prevention
- 1. Fluids and hydration
- a. Promote excretion of uric acid and phosphorus; increase glomerular filtration rate (GFR) and renal blood
- flow.
- b. Hydration at a rate of .2 l/m2/day should start 24 h before chemotherapy.
- c. Urine output goal of 3 ml/kg/h should be maintained. Diuretics may be needed to maintain this urine
- output.

- 2. Allopurinol
- a. A xanthine analog which blocks conversion of xanthine and hypoxanthine to uric acid; works as a
- competitive inhibitor of xanthine oxidase.
- b. Does not remove preformed uric acid.
- c. Slow reduction in uric acid levels.
- d. Decreased risk of uric acid crystallization in kidney tubules.
- e. Adverse effects include hypersensitivity reaction and a build up of xanthine and hypoxanthine, which may
- lead to renal insufficiency as well.

- 3. Rasburicase
- a. Indicated for patients at high risk of TLS.
- b. Assess patient's G6PD status or risk of having G6PD, as may cause methemoglobinemia or severe
- hemolytic anemia.
- c. May require reinitiation of allopurinol several days after rasburicase.

Management/objective	Guidelines
Aggressive hydration	Usually 2–4 times maintenance (alkalinization is avoided so as not to precipitate xanthine calculi and cause acute kidney injury)
Diuresis	Furosemide 0.5–1 mg/kg Mannitol 0.5 g/kg can be used if patient has oliguria unresponsive to increased hydration and furosemide
Uric acid reduction	(1) Allopurinol 300 mg/m^2/day or 10 mg/kg/day PO (maximum dose 800 mg/day) or 200 mg/m^2/day IV (maximum dose 600 mg/day) may be used if available; (2) Rasburicase (recombinant urate oxidase) 0.15–0.2 mg/kg/day IV, the dose can be repeated
Leukocyte reduction	Leukapheresis or exchange transfusion (for infants) can be used at any WBC count if the patient is symptomatic. In asymptomatic patients, leukapheresis should be considered if the initial white cell count is greater than 200,000/mm^3 in AML or 300,000/mm^3 in ALL or CML
Transfusion	Platelet transfusion to keep platelet count over 20,000/mm^3 to decrease the risk of intracranial hemorrhage. Avoid packed RBC transfusions if cardiovascularly stable, because it increases blood viscosity. Fresh frozen plasma transfusion and administration of vitamin K can be considered if coagulopathy is present prior to any invasive procedures
Chemotherapy	Chemotherapy should be started when patient is stabilized and has adequate urine output
Dialysis	Dialysis is indicated for progressive renal failure with potassium >6 mEq/l, phosphate >10 mg/dl, oliguria, anuria, or volume overload unresponsive to the above measures
Monitor	Electrolytes; calcium, phosphorus, potassium, uric acid, BUN, and creatinine every 4–12 h depending upon risk of TLS. Complete blood counts 1–2 times per day. Respiratory, CNS, and cardiac monitoring if hyperkalemia or hypocalcemia are present
Imaging	Brain CT with contrast if no renal insufficiency in the presence of neurologic symptoms or signs. MRI, MRA, or MRV should be carried out if thrombosis is suspected

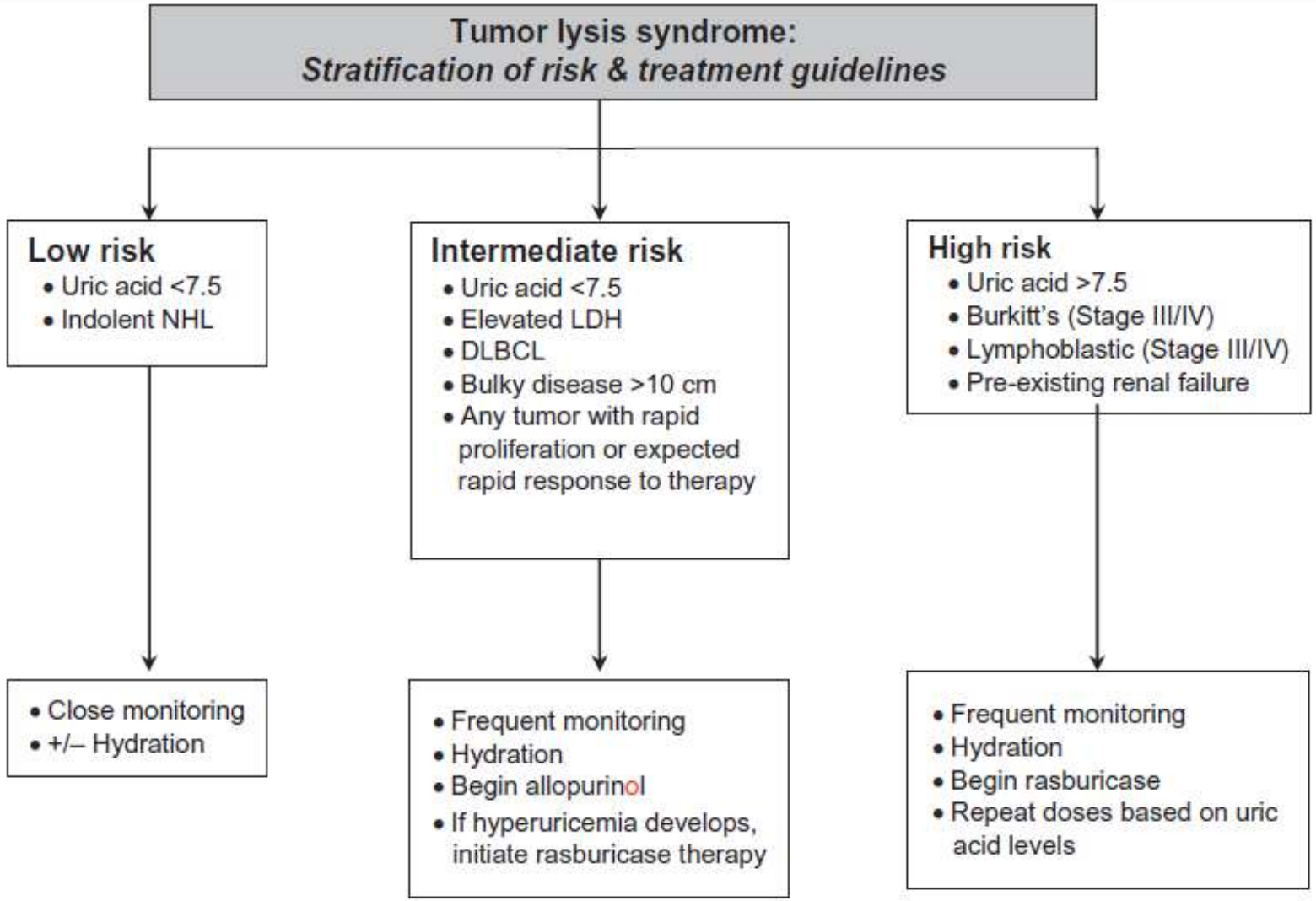

FIGURE 32.1 Treatment algorithm for the prevention and management of hyperuricemia. The treatment approach for low-risk patients is close observation with or without hydration. For those with intermediate risk, rasburicase is recommended if hyperuricemia develops despite prophylactic treatment with allopurinol. Vigorous hydration is recommended for all patients in the intermediate-to-high-risk groups, or those with diagnosed TLS. The use of rasburicase is recommended for the treatment of patients with hyperuricemia associated with diagnosed TLS, or in the initial management of patients considered to be at high risk of developing TLS. TLS, tumor lysis syndrome; NHL, non-Hodgkin lymphoma; LDH, lactate dehydrogenase; DLBCL, diffuse large B-cell lymphoma. *Adapted from Hochberg and Cairo (2008). Reprinted with permission.*

- Management of the Various Metabolic Derangements in TLS
- Hyperuricemia
- 1. Pharmacologic treatment should be based on risk stratification as outlined in Figure 32.1, which shows a
- treatment algorithm for the prevention and management of hyperuricemia.
- a. For low-risk patients: Observation and frequent laboratory monitoring are required. Allopurinol can be
- initiated as first-line therapy at diagnosis.
- b. For intermediate-risk patients: Allopurinol should be initiated as first-line therapy at diagnosis. Rasburicase
- should be considered if laboratory or clinical evidence of TLS is present despite allopurinol.
- c. For high-risk patients: Consider the use of rasburicase at diagnosis for tumors with high proliferative index,
- large tumor burden, or tumors that are highly chemo-sensitive. Rasburicase should also be considered as
- first-line therapy for patients with clinical evidence of TLS despite risk stratification. Rasburicase must be
- used with caution in patients with unknown G6PD status and/or at high risk for having G6PD deficiency.

- 2. Hydration .2 l/m2/day should start before chemotherapy and urine output goal of .100 ml/m2/h should be maintained during chemotherapy. Strict measurement of intake and output should be carried out every 24 h.
- Diuretics may be needed to maintain this urine output (i.e., furosemide 0.5-1 mg/kg/dose or mannitol 0.5 g/kg of the 25% solution over 5-10 min repeated every 6 h as needed).

- Hyperkalemia
- 1. Potassium should be avoided unless dangerously low until tumor lysis is controlled.
- 2. Mild (‚6 mEq/l) and asymptomatic:
- a. Hydration and diuretics as described in hyperuricemia.
- b. Sodium polystyrene sulfonate (kayexelate) at dose of 1 g/kg every 6 h with sorbitol 50-150 ml will remove
- 1 mEq of potassium per liter per gram of resin over 24 h.

- 3. Moderate to severe hyperkalemia:
- a. Obtain an EKG.
- b. Rapid insulin (0.1 U/kg/h) plus glucose (dextrose 0.5 g/kg/h); in emergency cases, 50% dextrose can be
- used at 1 ml/kg through a central line. Monitor serum glucose closely.
- c. For life-threatening arrhythmias IV calcium gluconate (100-200 mg/kg) or calcium chloride (10 mg/kg)
- slow IV infusion rate. The onset of action is within minutes and duration of activity lasts about 30 min
- (cannot be administered in the same line as NaHCO3).
- d. NaHCO3 to stabilize myocardial cell membrane and to reverse acidosis; 1-2 mEq/kg IV. For every increase
- of 0.1 pH unit, potassium is decreased about 1 mEq/l. Onset of action is within 30 min and duration of
- action lasts several hours.
- e. Dialysis should be considered while these rescuing approaches are underway.

- Hyperphosphatemia
- 1. Lymphoblasts contain four times the amount of phosphate present in normal lymphocytes; consider a low phosphate diet.
- 2. Aluminum hydroxide 150 mg/kg/day divided into doses every 4-6 h should be administered. This will
- prevent absorption of oral phosphate intake, but has little direct effect on lowering serum phosphate.
- Sevelamer hydrochloride (RenaGel), a noncalcium phosphate binder (400 mg twice daily for older children)
- can also be used.
- 3. Hydration necessary to maintain a urine output of >3 ml/kg/h.
- 4. Dialysis may be necessary to lower serum phosphate and prevent metastatic calcium deposition.

- Hypocalcemia
- 1. As the product of serum calcium and phosphate increases over 60 due to hyperphosphatemia, a compensatory hypocalcemia may occur to maintain the calcium phosphate product at 60. At a calcium×phosphate product of >60 renal calcification can occur and exacerbate renal damage.
- 2. For symptomatic hypocalcemia (e.g., tetany), 10 mg/kg of elemental calcium (i.e., 0.5-1.0 ml/kg of 10%
- calcium gluconate) should be given. Calcium administration should be discontinued when symptoms resolve.
- Dialysis should be carried out if hyperphosphatemia persists. (Caution: Do not administer calcium in the same line as NaHCO3.)

- Renal Dysfunction from Tumor Lysis
- Mechanisms of Renal Dysfunction
- 1. Precipitation of urates in the acid environment of the renal tubules.
- 2. Precipitation of hypoxanthine when the urine pH exceeds 7.5.
- 3. Increase in the hypoxanthine levels after starting treatment with allopurinol.
- 4. Precipitation of calcium phosphate in renal microvasculature and renal tubules when the product of serum
- calcium and phosphate values exceeds 60.

- Indications for Dialysis Include the Following
- 1. Presence of hyperphosphatemia (.>6 mg/dl) and hypercalcemia which promotes deposition in renal
- interstitium and tubular system, exacerbating kidney damage.
- 2. An estimated GFR less than 50%.
- 3. Persistent hyperkalemia with QRS interval widening and/or level exceeding 6 mEq/l.
- 4. Severe metabolic acidosis.
- 5. Volume overload unresponsive to diuretic therapy.
- 6. Anuria and overt uremic symptoms (i.e., encephalopathy).
- 7. Severe symptomatic hypocalcemia.
- 8. Hypertension (BP.150/90) and inadequate urine output at 10 h from start of treatment.
- 9. Congestive heart failure.

- Hemodialysis or hemofiltration should be used when renal failure occurs. Continuous renal replacement therapy (CRRT) may be used for hemodynamically unstable patients because it is less likely to exacerbate hypotension.
- CRRT is not as effective for the treatment of hyperphosphatemia. Peritoneal dialysis should not be used.
- Dialyzable chemotherapy, such as cyclophosphamide, is given immediately after dialysis and not before. Renal
- dialysis usually needs to be repeated every 12 h while there is continuous rapid tumor lysis.

- CARDIOTHORACIC EMERGENCIES

- Superior Vena Cava Syndrome and Superior Mediastinal Syndrome
- Superior vena cava syndrome (SVCS) consists of the signs and symptoms of superior vena cava (SVC)
- obstruction due to compression or thrombosis. This condition is frequently due to a large anterior mediastinal mass compressing the SVC. Rapid growth of the mediastinal mass does not permit the development of effective collateral circulation to compensate and results in the signs and symptoms of compression of the SVC.
- Superior mediastinal syndrome (SMS) consists of SVCS with tracheal compression.
- The trachea and main stem bronchus are more compressible in children, making them more susceptible to
- SMS. In pediatrics, the terms SVCS and SMS are often used synonymously.

- Etiology
- 1. Intrinsic causes: vascular thrombosis following the introduction of a catheter, intravascular tumor thrombosis (Wilms, lymphoma).
- 2. Extrinsic causes: malignant anterior mediastinal tumors
- a. Hodgkin lymphoma.
- b. Non-Hodgkin lymphoma.
- c. Teratoma or other germ cell tumor.
- d. Thyroid cancer.
- e. Thymoma.

- Clinical Features
- 1. Superior vena cava syndrome:
- a. Swelling, plethora, and cyanosis of the face, neck, and upper extremities.
- b. Suffusion of the conjunctiva.
- c. Engorgement of collateral veins.
- d. Altered mental status.
- 2. Superior mediastinal syndrome:
- a. Respiratory symptoms: cough, hoarseness, dyspnea, orthopnea, wheezing, and stridor. Supine position
- worsens symptoms.
- b. Dysphagia.
- c. Chest pain.
- d. Altered mental status and syncope.

- Management
- 1. Extreme care is required in handling the patient. The following may precipitate respiratory arrest:
- a. Supine position (as for CT or operative procedures)—Do not place patient in recumbent position.
- b. Medications that cause intercostal muscle relaxation.
- c. Stress.
- d. Sedation (conscious sedation, anxiolytics, or general anesthesia). The patient may have to be intubated.
- Extubation may not be possible until the anterior mediastinal mass has significantly decreased in size.
- Extracorporeal membrane oxygenation may be required if intubation is not possible.

- 2. Diagnosis should be made quickly in the least invasive manner.
- a. Radiograph of the chest and CT (if tolerated).
- b. Screening blood work such as CBC, LDH, uric acid, α-fetoprotein, and β-hCG (to screen for germ cell
- tumors and lymphoma).
- c. Echocardiogram, to assess anesthesia risk, cardiac function and for possible intravascular thrombus if no
- evidence of mass on chest radiograph.
- d. Determine anesthesia risk. If high risk, perform the least invasive technique with local anesthesia (bone
- marrow, pleurocentesis, pericardiocentesis, lymph node biopsy, or fine-needle aspirate). If low risk use
- sedation or anesthesia and monitor closely.

◦ 3. Therapy:

◦ a. Establishing a tissue diagnosis may not be possible and patients may need empiric treatment as a life-saving

◦ measure. First-line treatment in emergent situations is high-dose steroids, although they may confound the

◦ diagnosis. Prednisolone 60 mg/m2/day (2 mg/kg/day) or methylprednisolone 48 mg/m2/day (1.6 mg/kg/day)

◦ divided into two daily doses should be employed. This will treat hematologic malignancies and decrease airway

◦ edema. The patient should undergo biopsy as soon as the mass shrinks and the patient is stable.

◦ b. If poor response to steroids, chemotherapy such as vincristine, cyclophosphamide with or without an

◦ anthracycline can be added. Tumor-specific chemotherapy should be instituted after a biopsy has been obtained.

◦ c. If a solid tumor not responsive to steroids or chemotherapy, emergent radiation can be performed.

- d. For symptomatic venous thrombosis with no evidence of hemorrhage, anticoagulation can be initiated
- using systemic or low-molecular-weight heparin (LMWH):
- i. Unfractionated heparin can be started with a 75 U/kg bolus followed by 18 U/kg/h (for children) to
- 28 U/kg/h (infants) continuous infusion. Titrate to a goal-activated partial thromboplastin time of
- 60-85 s or anti-Xa level of 0.3-0.7 U/ml.
- ii. LMWH 1 mg/kg every 12 h. Titrate to a goal anti-Xa level of 0.5-1 U/ml.

- ABDOMINAL EMERGENCIES

- 1. Esophagitis: the most common gastrointestinal (GI) problem in oncology patients.
- 2. Gastric hemorrhage: especially in patients on corticosteroid therapy.
- 3. Typhlitis: seen primarily in patients with prolonged neutropenia or at new diagnosis of leukemia.
- 4. Perirectal abscess: in prolonged neutropenia.
- 5. Hemorrhagic pancreatitis: especially in patients on asparaginase therapy.
- 6. Massive hepatic enlargement from tumor: especially in infants with stage IVS neuroblastoma.

TABLE 32.3 Evaluation and Management of Common Causes of Abdominal Pain

Diagnosis	Signs and symptoms	Clinical set-up	Evaluation	Management
Bowel obstruction	Pain Decreased bowel sounds	Tumor Adhesions	Abdominal radiograph	Bowel rest/NG Surgical consultation
Constipation/ileus	Hard stools or no stool Pain	Narcotics Postoperative Vincristine Dehydration	Abdominal radiograph	Stool motility agents Stool softeners, bulking agents IV hydration
Gastritis/esophagitis	Gastric/throat pain Metallic taste	Chemotherapy, steroids *Candida*	Oral examination	Oral or IV antacid Antifungal
Hepatic enlargement/ VOD	RUQ mass	Neuroblastoma Stage 4S	CT, urine VMA/HVA	Chemotherapy
Pancreatitis	RUQ pain Emesis	Asparaginase Steroids	Amylase, lipase US/CT for pseudocyst	Bowel rest/NG
Perirectal abscess	Erythema Induration Pain with defecation	Severe myelosuppression	Perirectal examination	Broad-spectrum antibiotics (Gram-negative and anaerobes) Sitz baths (4 times a day)
Typhlitis/colitis	Acute abdomen/RLQ pain Diarrhea Hypotension Bloody diarrhea	Severe myelosuppression Acute leukemia	Abdominal radiograph or CT (free air or thickened bowel wall) Stool cultures	Nothing by mouth Bowel rest/NG Surgical consultation Broad-spectrum antibiotics (Gram-negative, anaerobes, fungus)
Veno-occlusive disease	RUQ mass Edema Weight gain Jaundice	Post-transplant 6-Thioguanine, Actinomycin Gemtuzumab	US for reversal of flow Bilirubin Weight checks	Stop inciting agents Defibrotide

RUQ, right upper quadrant of abdomen; RLQ, right lower quadrant of abdomen; US, ultrasound; NG, nasogastric tube suctioning.

- Evaluation and Diagnosis of Abdominal Emergencies
- 1. History regarding onset, timing, location, and radiation of pain.
- 2. Observation and gentle examination including mouth and perirectal area in particular. If rectal examination is deemed necessary it should be performed very gently.
- 3. The classic signs of an acute abdomen may be muted in a neutropenic patient or a patient on steroids.
- 4. Serial blood counts to evaluate for hemorrhage, neutropenia, infection.
- 5. Blood, stool, and urine cultures as indicated.
- 6. Laboratory tests, liver enzymes, bilirubin, amylase, lipase, electrolytes.
- 7. Vital signs monitoring.
- 8. Abdominal radiography: ultrasonography, CT, and magnetic resonance imaging (MRI) as indicated.

- Typhlitis
- Typhlitis, a necrotizing colitis often localized in the cecum, occurs in the setting of severe neutropenia, particularly in patients with leukemia and in stem cell transplant recipients. It should be strongly suspected in patients with right lower quadrant pain or the development of a partially obstructive right lower quadrant mass.
- Typhlitis is the result of bacterial or fungal invasion of the mucosa and can quickly progress from inflammation to full-thickness infarction to perforation, peritonitis, and septic shock.

- Etiology
- 1. The responsible pathogens include Pseudomonas species, Escherichia coli, other Gram-negative bacteria,
- Staphylococcus aureus, α-hemolytic Streptococcus, Clostridium, Aspergillus, and Candida.
- 2. Typhlitis in patients receiving chemotherapy is linked to mucosal injury caused by cytotoxic chemotherapeutic agents

Diagnosis

Typhlitis is usually diagnosed clinically when a neutropenic patient presents with:

1. Right lower quadrant pain.

2. Physical examination may reveal an absence of bowel sounds, bowel distention, tenderness on palpation maximal in the right lower quadrant, or a palpable mass in the right lower quadrant. Serial abdominal examinations are required.

3. Imaging studies may aid in the diagnosis of typhlitis:

a. Radiograph of the abdomen may reveal pneumatosis intestinalis, free air in the peritoneum or bowel wall thickening.

b. Ultrasonography may reveal thickening of the bowel wall in the region of the cecum and is becoming a more commonly used nonradiation modality to image for typhlitis.

c. CT scan is the definitive imaging study and may demonstrate diffuse thickening of the cecal wall.

- Treatment
- 1. Medical management is the initial treatment, consisting of: a. Discontinuation of oral intake.
- b. Nasogastric tube to suction. c. Broad-spectrum antibiotics (anaerobic and Gram-negative coverage) and anti-fungals. d. Intravenous fluid and electrolytes. e. Packed red cell and platelet transfusions, as indicated. f. Vasopressors, as needed (hypotension is associated with a poor outcome).
- 2. Indications for surgical intervention: a. Persistent GI bleeding despite resolution of neutropenia and thrombocytopenia. b. Evidence of free air in the abdomen on abdominal radiograph (indicating perforation).
- c. Clinical deterioration requiring fluid and pressor support, indicating uncontrolled sepsis from bowel
- infarction. d. Surgery consists of removing necrotic portions of the bowel and diversion via colostomy. Healing can occur with fibrosis and stricture formation. e. Mortality is related to bowel perforation, bowel necrosis, and sepsis.

- Perirectal Abscess
- Inflammation and infection of the rectum and perirectal tissue occur commonly in patients receiving chemotherapy or radiation therapy, especially in patients with prolonged neutropenia. Most abscesses are caused not by a single organism but rather by a combination of aerobic organisms, such as staphylococci, streptococci, E. coli, Pseudomonas, and anaerobic Gram-positive and -negative organisms.
- Presentation includes anorectal pain, tenderness, and painful bowel movements. An abscess or draining fistula may be present; however, in the neutropenic patient, pus will be absent and the patient will present with a brawny edema and dense cellulitis.

- Management
- 1. Initial therapy with intravenous antibiotics to cover Gram-negative organisms and anaerobes.
- 2. Granulocyte colony-stimulating factor to shorten period of neutropenia.
- 3. Sitz baths four times a day, and meticulous attention to perirectal hygiene.
- 4. Surgical incision and drainage of obviously fluctuant areas or draining fistulas that do not resolve with
- medical management.

- RENAL EMERGENCIES

- Oliguria/Anuria
- Differential Diagnoses
- • Prerenal: septic shock, dehydration, emesis, diarrhea, decreased oral intake, metabolic abnormalities from
- tumor lysis.
- • Postrenal: bulky abdominopelvic tumors with obstruction, hemorrhagic cystitis.
- • Renal insufficiency: chemotherapy agents, contrast dyes, anti-infectives.
- Evaluation
- • BUN, creatinine, electrolytes.
- • Close monitoring of all intake and output.
- • CT or ultrasound (US) of abdomen/pelvis.

- Therapy
- • Vigorous hydration for prerenal etiologies including BK viremia.
- • Decompression of obstructed kidney with stenting or catheter placement in postrenal etiologies.
- • Treatment of underlying tumor with chemotherapy, surgery, or radiation to decrease outflow obstruction.
- • Avoidance of nephrotoxic agents, IV contrast, and appropriate renal dosing of medications.
- • With significant electrolyte abnormalities, fluid overload or true anuria, consideration of dialysis may be
- indicated.

- Hypertension
- Definition
- • Systolic or diastolic blood pressure outside the 95th percentile for age, gender, and height.
- Etiology
- • Secondary to pain or anxiety, and often transient.
- • Secondary to tumor compression of renal parenchyma leading to increased renin production (secondary
- hyperaldosteronism).

- • Secondary increased renin production from tumors (e.g., pheochromocytoma, Wilms' tumor, neuroblastoma).
- • Secondary to medications: steroids, anti-infectives, calcineurin inhibitors.
- • Renal vein thrombosis.
- • Increased intracranial pressure (ICP).
- Symptoms
- • Symptoms may include headache, irritability, lethargy, confusion, and, if untreated, seizures, posterior
- reversible encephalopathy syndrome (PRES).

- Treatment
- • Acute hypertension:
- • Hydralazine (0.2-0.6 mg/kg/dose IV).
- • Nicardipine (0.5-1 μg/kg/min infusion to be titrated to desired blood pressure).
- • Labetalol (0.2-1 mg/kg/dose IV, to be avoided in patients with bronchospasm or diabetes).
- • Sublingual nifedipine (5-10 mg/dose for children weighing .10 kg).
- • Oral clonidine (0.05-0.1 mg/dose).
- • Chronic hypertension:
- • Amlodipine (0.1 mg/kg per dose, or 2.5-5 mg/day).
- • Consider ACE inhibitors or beta-blockers.
- • Hypertension from fluid overload:
- • Furosemide (0.5-1 mg/kg).

◦NEUROLOGIC EMERGENCIES

- Neurologic emergencies, such as seizure, alterations in mental status (AMS), cerebrovascular accidents
- (CVAs), spinal cord compression, and increased ICP occur in over 10% of pediatric oncology patients. Initial
- intervention for acute neurologic deterioration requires immediate stabilization of the patient.

- Evaluation and Diagnosis of Neurologic Emergencies
- 1. Detailed history including current medications, recent chemotherapy and radiation therapy, prior events.
- 2. Thorough physical and neurologic examination, pulse oximetry, vital signs.
- 3. Laboratory tests including blood count, electrolytes, ammonia, liver, toxicology screen, and renal function tests.
- 4. Head CT acutely, MRI/magnetic resonance angiography (MRA).
- 5. Spinal tap.
- 6. Electroencephalogram

- Differential Diagnosis
- • Seizures: CNS tumors, intrathecal chemotherapy, metabolic derangements.
- • Raised ICP: CNS tumors, shunt obstruction, pseudotumor cerebri, infection, CVA.
- • CVA: Asparaginase, hyperleukocytosis, coagulopathy/hemorrhage, radiation-induced vasculopathy.
- • AMS: CNS tumor, opiates, benzodiazepines, steroids, intrathecals, high-dose cytarabine or methotrexate,
- ifosfamide, nelarabine, postictal, CVA, CNS infection, metabolic derangements, postradiation somnolence.

- Management
- 1. Stabilize the patient: oxygen and hydration as needed.
- 2. Stop any intravenous infusions, especially chemotherapy, narcotics.
- 3. Transfuse platelets if thrombocytopenic.
- 4. Start broad-spectrum antibiotics after blood culture is obtained, a spinal tap can be performed once the CT reveals normal ventricular size.
- 5. If actively having seizures administer ativan or dilantin load.
- 6. Emergent head CT to look for CNS bleed, hydrocephalus, herniation, or mass, MRI/MRA/magnetic resonance venography (MRV), when available, to look for white matter changes and vascular issues. If nonhemorrhagic stroke is found on MRI, thrombolysis and anticoagulation should be considered.

- Spinal Cord Compression
- Incidence and Etiology
- • Three to five percent of children with cancer develop acute spinal cord or cauda equina compression.
- Sarcomas account for about half of the cases of spinal cord involvement in childhood. The remainder are
- caused by neuroblastoma, germ cell tumor, lymphoma, leukemia, and drop metastasis of CNS tumors.
- • The spinal cord can be compressed by tumor in the epidural or subarachnoid space or by metastases within
- the cord parenchyma.

- Pathophysiology
- • Direct extension of the tumor.
- • Metastatic spread to the vertebrae with secondary cord compression.
- • Spread to the epidural space via infiltration of the vertebral foramina.
- • Subarachnoid spread down the spinal cord from primary CNS tumor (such as medulloblastoma).

- Clinical Presentation
- • Back pain with localized tenderness occurs in 80% of patients.
- • Incontinence, urinary retention, and other abnormalities of bowel or bladder function are not frequent if spinal compression is diagnosed early.
- • Loss of strength and sensory deficits with a sensory level may also occur.
- • Any child with cancer and back pain should be presumed to have spinal cord involvement until further
- workup indicates otherwise.

- Evaluation
- • A thorough history and neurologic examination should be included in the evaluation.
- • Spinal radiographs are useful if the compression is due to vertebral metastases but they will miss epidural
- disease in 50% of cases.
- • MRI with and without gadolinium is necessary to detect the presence and extent of epidural involvement.
- • Cerebrospinal fluid analysis is important in the evaluation of subarachnoid disease, but it is not helpful in
- localizing epidural disease.

- Treatment
- • Because the potential for permanent neurologic damage is high, it is crucial to initiate treatment immediately.
- • Dexamethasone is initiated to decrease local edema, prior to diagnostic studies.
- • In the presence of neurologic abnormalities, immediately start dexamethasone 1-2 mg/kg/day loading
- dose. Follow with 1.5 mg/kg/day divided every 6 h and obtain emergent MRI.
- • With back pain and the absence of neurologic symptoms, start dexamethasone 0.25-1 mg/kg/dose every
- 6 h and perform MRI within 24 h.
- • If an epidural mass is identified, treatment is aimed at rapid decompression. Chemotherapy, radiation
- therapy, or surgical decompression may be used.

- • Specific chemotherapy can be instituted in addition to the use of dexamethasone in lymphoma, leukemia,
- and neuroblastoma.
- • If tumor is known to be radiosensitive, give local radiation including the full volume of the tumor plus one
- vertebra above and below the lesion. Consult a radiation oncologist for daily dosing fractions and total
- dose.
- • Surgical emergent laminotomy or laminectomy may be indicated for paralysis requiring rapid
- decompression, especially in lesions expected to be less radioresponsive (e.g., sarcoma) or no symptomatic
- improvement with emergent steroids, chemotherapy, and/or radiation.

- ENDOCRINE EMERGENCIES

- Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)
- Etiology
- 1. Involves continuous pituitary release of antidiuretic hormone (ADH), irrespective of plasma osmolality.
- 2. Leads to significant hyponatremia, serum hypo-osmolality, and water intoxication.
- 3. Results from physiologic stress, pain, surgery, mechanical ventilation, infections, CNS and pulmonary lesions, lymphomas, and leukemias.
- 4. Occurs as a side effect of vincristine, vinblastine, cyclophosphamide, ifosfamide, cisplatin, and melphalan.
- 5. Occurs in overhydration with hypotonic fluids, diabetes insipidus with free water replacement, and cerebral
- salt wasting.

- Clinical Features
- • Oliguria.
- • Weight gain.
- • Often asymptomatic.
- • Early symptoms can include fatigue, headache, and nausea.
- • Late manifestations include lethargy, confusion, hallucinations, seizures, and coma.
- Laboratory Features of SIADH
- • Low serum osmolality (<280 mOsm/l).
- • High urine osmolality (>500 mOsm/l).
- • Urine to serum osmolality ratio >1.
- • Hyponatremia (sodium, <130 mEq/l).
- • Increased urine specific gravity.

- Treatment
- 1. Fluid restriction.
- 2. Furosemide 1 mg/kg should be administered to increase diuresis of free water and reduce the impact of the excess ADH.
- 3. Hydration with normal saline limited to insensible losses (500 ml/m2/24 h) plus ongoing losses.
- 4. In cases of severe neurologic involvement (seizures or coma), hydrate carefully with hypertonic saline 3%. The rate of sodium correction should be limited to 2 mEq/l/h over the first 2 h. Subsequent to that the rate of correction should target a change of serum sodium by 10 mEq over the first 24 h and 18 mEq by 48 h of
- treatment.
- Too rapid correction may lead to further permanent neurologic sequelae.

- Hypercalcemia of Malignancy
- Etiology
- 1. Osteolytic bone lesions (particularly in T-cell leukemia and lymphoma).
- 2. Bone demineralization secondary to parathyroid-like hormone (PTHrP) produced by tumors (paraneoplastic syndrome).
- 3. Immobilization.
- 4. Defect in renal excretion.

- ## Clinical Features
- Patients typically become symptomatic when serum calcium exceeds 12 mg/dl.
- • Anorexia, nausea, vomiting, and constipation.
- • Weakness.
- • Coma.
- • Pruritis.
- • Bone pain.
- • Polyuria, polydipsia, nephrogenic diabetes insipidus.

- • Bradycardia, arrhythmias.
- • Dehydration, impaired renal function.
- • Disseminated intravascular coagulation.

- Treatment
- 1. Dehydration and electrolyte disturbances should be corrected. Stop calcium-containing medications.
- 2. Renal calcium excretion should be increased by inducing diuresis with normal saline at two- to threefold
- maintenance and furosemide 1-2 mg/kg/dose every 6 h.
- 3. Calcium mobilization from bone should be decreased by
- a. Bisphosphonates, such as pamidronate 0.5-1 mg/kg IV over 4-6 h with very close monitoring of serum calcium, phosphate, and magnesium for 2 weeks.
- b. Prednisone 1.5-2.0 mg/kg daily (in lymphoproliferative disorders).

- Adrenal Insufficiency
- Etiology
- 1. Secondary to significant prior corticosteroid exposure.
- 2. During periods of critical illness, trauma, surgery, or infection.
- 3. Tissue resistance to steroids.
- 4. Adrenal gland failure.
- 5. Radiation or surgically induced impairment of cortisol synthesis due to injury to the adrenal glands.
- Clinical Features
- 1. Fatigue, dizziness, weakness, myalgia, nausea/vomiting.
- 2. Severe hypotension, shock.
- 3. Hyponatremia, hyperkalemia, metabolic acidosis with normal anion gap.

- Treatment
- 1. Glucocorticoid replacement therapy (hydrocortisone):
- a. Hydrocortisone at 100 mg/m2 and then 25 mg/m2 per dose given every 6 h for 7 days without taper.
- b. Fludrocortisone.
- c. Strict monitoring for hyperglycemia is critical during stress dosing of steroids.
- 2. Treatment includes interventions for sepsis and hypotension if warranted.
- 3. Consider checking cortisol levels as patient may need physiologic replacement once stress dosing is complete.


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